M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

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Date: October 6, 1999
To: Dockets Management Branch (HFA-305)

From: Melissa Lamb
Office of Generic Drugs

Subject: An Overview of the Office of Generic Drugs

This memorandum forwards overheads of a presentation to the Dockets Management Branch for inclusion in Docket 90S-0308. The following is information on the presentation for the Docket records:

Title of Presentation: An Overview of the Office of Generic Drugs

Presented for: U.S. Food & Drug Administration

Date Presented: 10/6/1999

Presented by: Gary J. Buehler

Number of Pages: 30

Melissa Lamb

Attachment

90S-0308

M671

AN OVERVIEW OF THE OFFICE OF GENERIC DRUGS

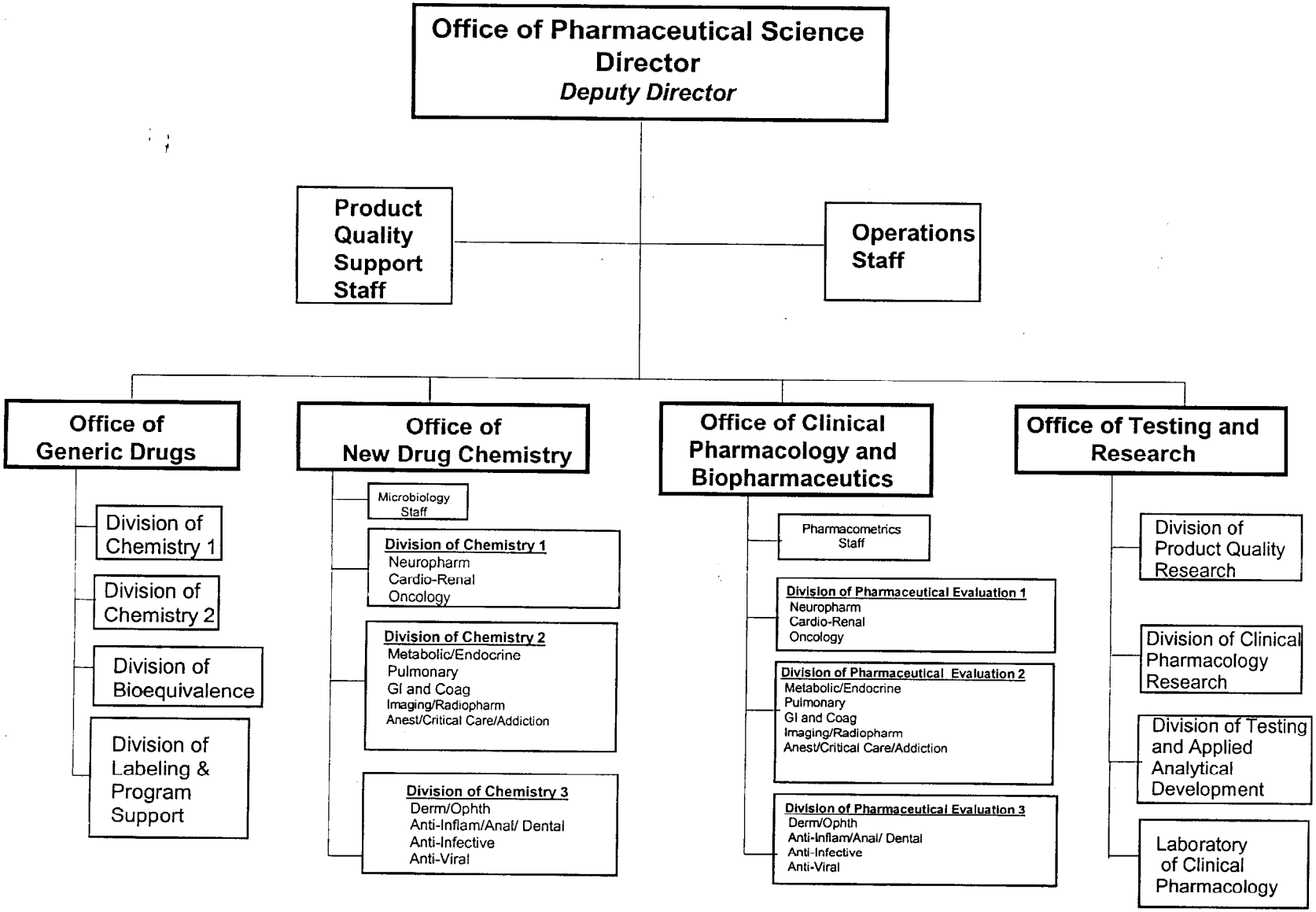
U.S. Food & Drug Administration

Douglas L. Sporn
Director
Office of Generic Drugs
October 6, 1999

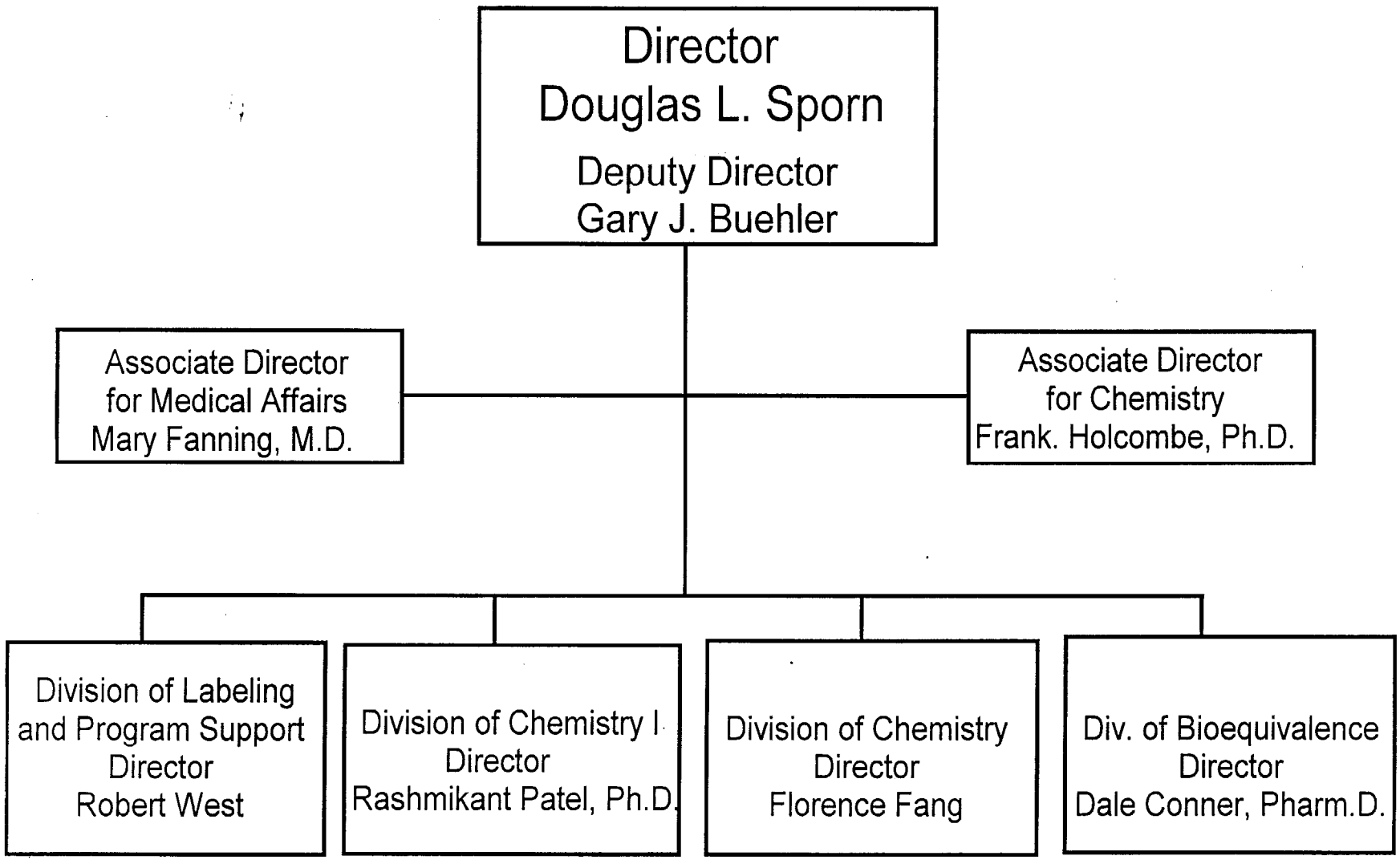
Outline

- OGD Structure
- Review Process Overview
- What is a Generic Drug
- Bioequivalence
- Patents/Exclusivity
- Orange Book

Deputy Center Director for Pharmaceutical Science



Office of Generic Drugs



OGD Personnel by Discipline

	On Board 9-28-99
Chemistry Reviewers	47
Bioequivalence Reviewers	26
Project Managers/Technician	15
Clerical	9
Labeling Reviewers	11
Management/Admin. Support	9
Microbiologists	4
Application Examiners	2
Medical Officer	1
Computer Specialist	2
Statistician	1
Total	127

Food and Drug Law History

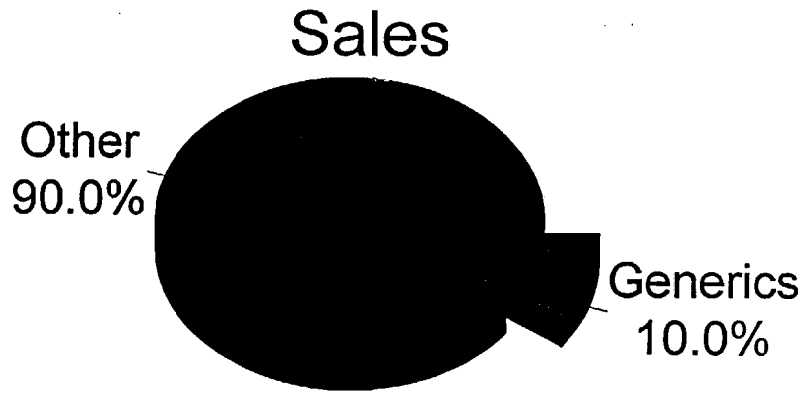
- Pure Food and Drug Act 1908
- Federal Food Drug and Cosmetic Act 1938
- Kefauver-Harris Drug Amendments 1962
- Drug Price Competition and Patent Term Restoration Act 1984

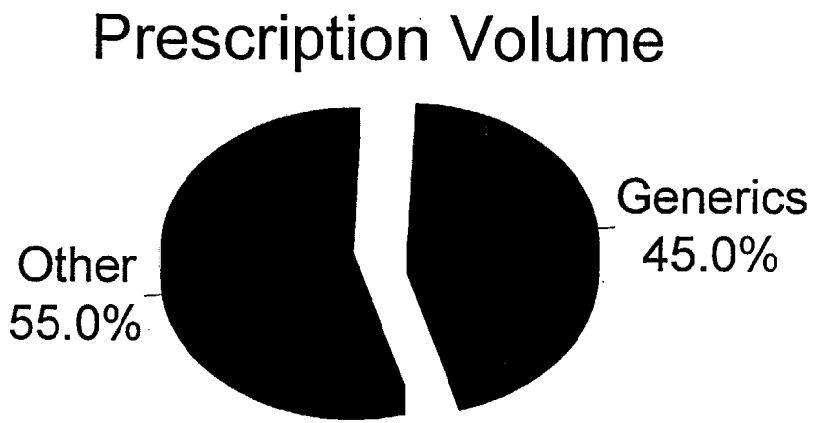
Legislation Spurred By:

Health Concerns	Economic Concerns
1906 Act	1984 Amendments
1938 Act	
1962 Amendments	

1995 Estimated Generic Market Share

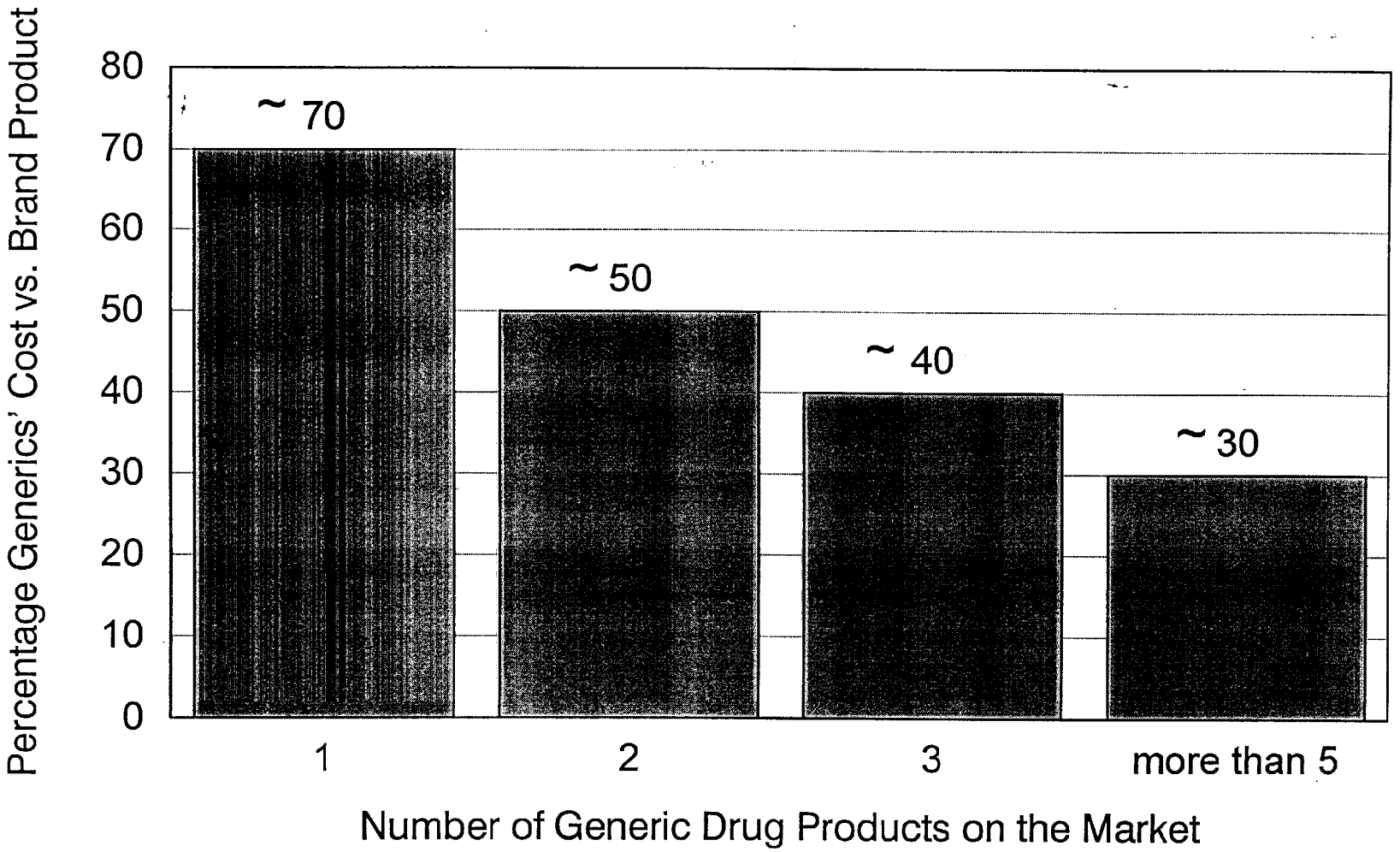
- U.S. Market = $60 billion (Approximate retail acquisition cost for Rx and Hospital Market)





- Generic Share of Market
  - 10% of $ = $6 billion
  - 45% of Rx and growing

Estimated Cost of Generic Drugs



Intent of the Drug Price Competition and Patent Term Restoration Act of 1984

(The Waxman-Hatch Amendments)

- Speed up FDA approval of Generic Drugs
- Make available high quality, low cost generics reducing health care costs
- Eliminate costly and unnecessary duplicative safety and efficacy studies
- Assure continued development of new drugs through special incentives

Legal Framework

Waxman Hatch Amendments

- Brand Name Incentives
  - Provides patent life up to 17 years and is eligible for 5 additional years.
    (GATT extends patents issued on or after June 8, 1995, to 20 years)
  - Exclusivity protection incentives for innovation
    - 5 year protection for new chemical entities
    - 3 year protection for a new salt or ester of previously approved active ingredient based on new clinical investigations
    - 3 year protection for a new use or dosage form

Legal Framework (cont.)

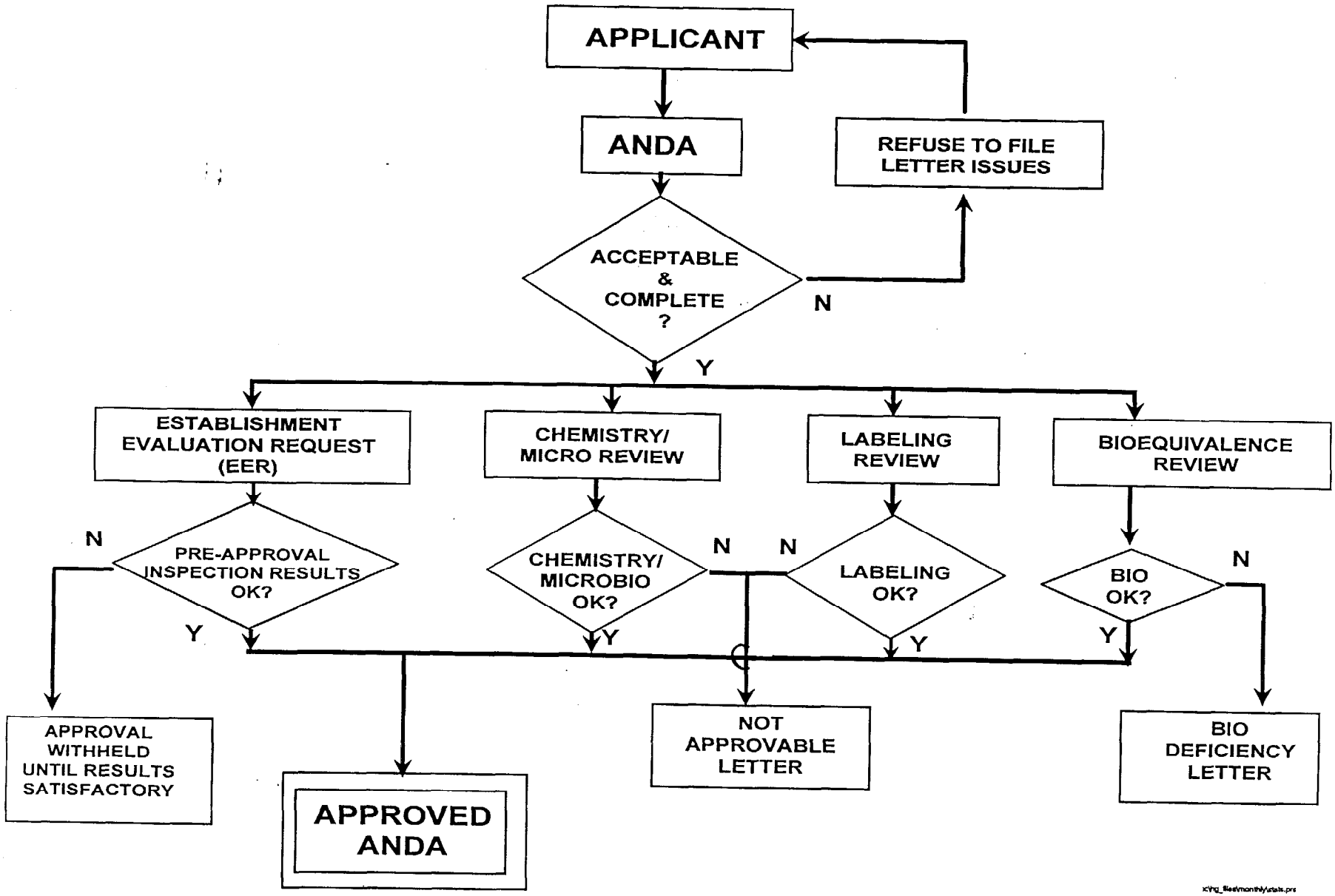
Waxman Hatch Amendments

- Generic Drug Incentives
  - All approved drug products eligible for generic competition
  - Eliminated requirement for duplicate clinical trials
  - Created a regulatory process for faster approval of generic drugs

NDA vs ANDA

Brand Name	Generic Drug
NDA Requirements	ANDA/AADA Requirements
1. Chemistry	1. Chemistry
2. Manufacturing	2. Manufacturing
3. Controls	3. Controls
4. Labeling	4. Labeling
5. Testing	5. Testing
6. Animal Studies	
7. Clinicals	6. Bioequivalence
8. Bioavailability	

Generic Drug Review Process



Criteria for ANDA Eligibility

- Same active ingredient(s)
- Same route of administration
- Same dosage form
- Same strength
- Same conditions of use
- Variations may be accommodated through a Suitability Petition

Generic Formulation

PHARMACEUTICAL AND THERAPEUTIC EQUIVALENCE

- Pharmaceutical Equivalence
  - √ Same active ingredient
  - √ Same strength
  - √ Same dosage form and route of administration
  - √ Comparable labeling

- Bioequivalence
  - √ In vivo measurement of active moiety (moieties) in biologic fluid, or
    - In vivo pharmacodynamic comparison
    - In vivo limited clinical comparison
    - In vitro comparison

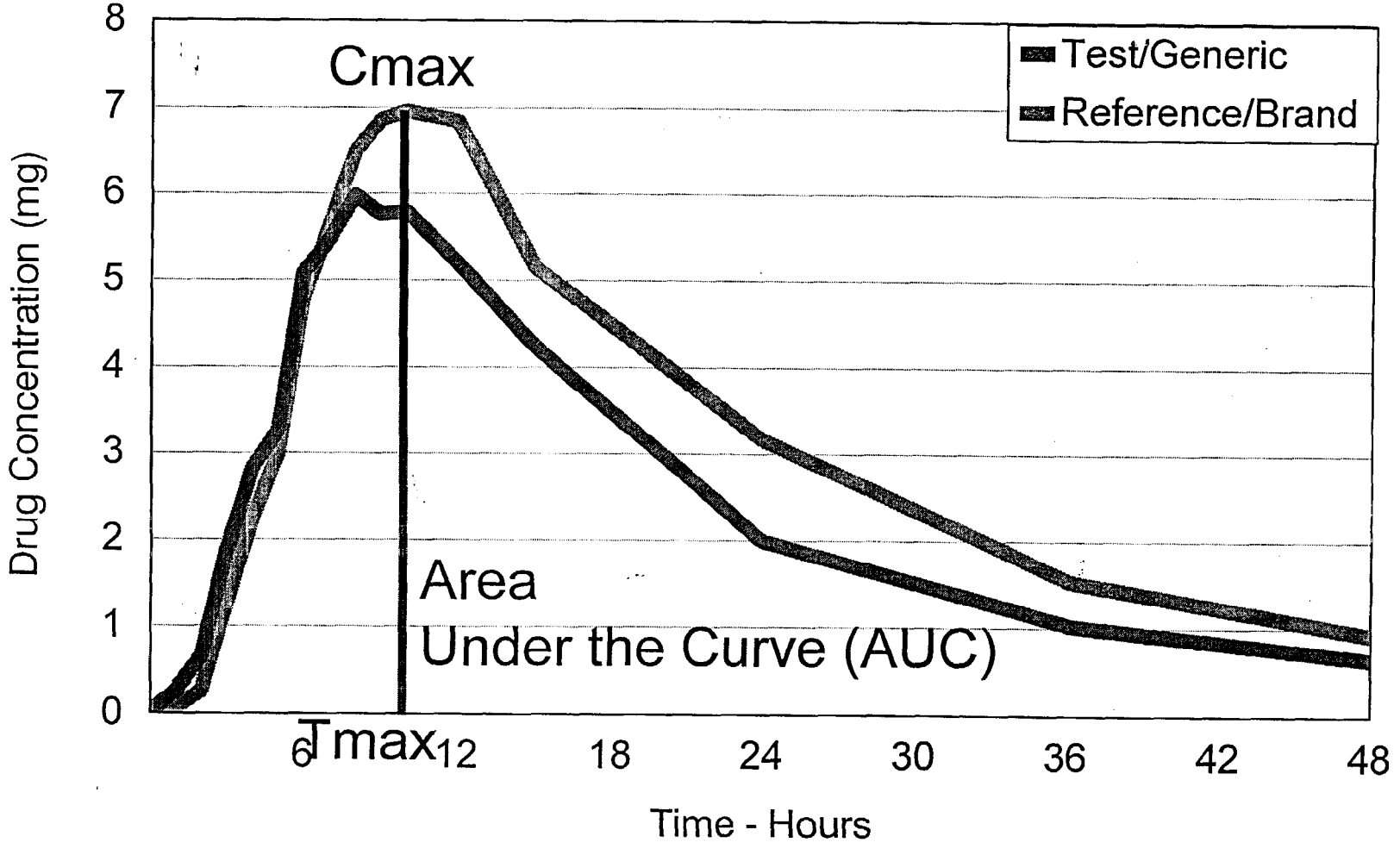
→THEN: THERAPEUTIC EQUIVALENCE

Definition of Bioequivalence

A generic drug is considered to be bioequivalent to the brand name drug if:

- The rate and extent of absorption do not show a significant difference from listed drug, or
- The extent of absorption does not show a significant difference and any difference in rate is intentional or not medically significant.

Mean Plasma Drug Level Versus Time



Bioequivalence Testing

- 20-24 healthy subjects (women and minorities encouraged)
- Crossover design
- Parameters measured
  - AUC (area under the curve)
  - Cmax (peak concentration)
  - Tmax (time to peak concentration)
- Statistical criteria: 90% confidence interval

Labeling

Same* as brand name labeling

"Sameness" eliminates confusion and unsupported claims by different manufacturers

* Generic drug labeling may differ to reflect differences in inactive ingredients, specific pharmacokinetic data, and how supplied information.

Patent Protection: Patent Filing

- Applies to NDA's only
- Delays final approval date of ANDA
- Patents covered:
  - Drug Product- Formulation, Composition
  - Drug Substance- Active ingredient
  - Method of Use- Indication
- Filing requirement: NDA's and some supplements
- Published in "Orange Book"

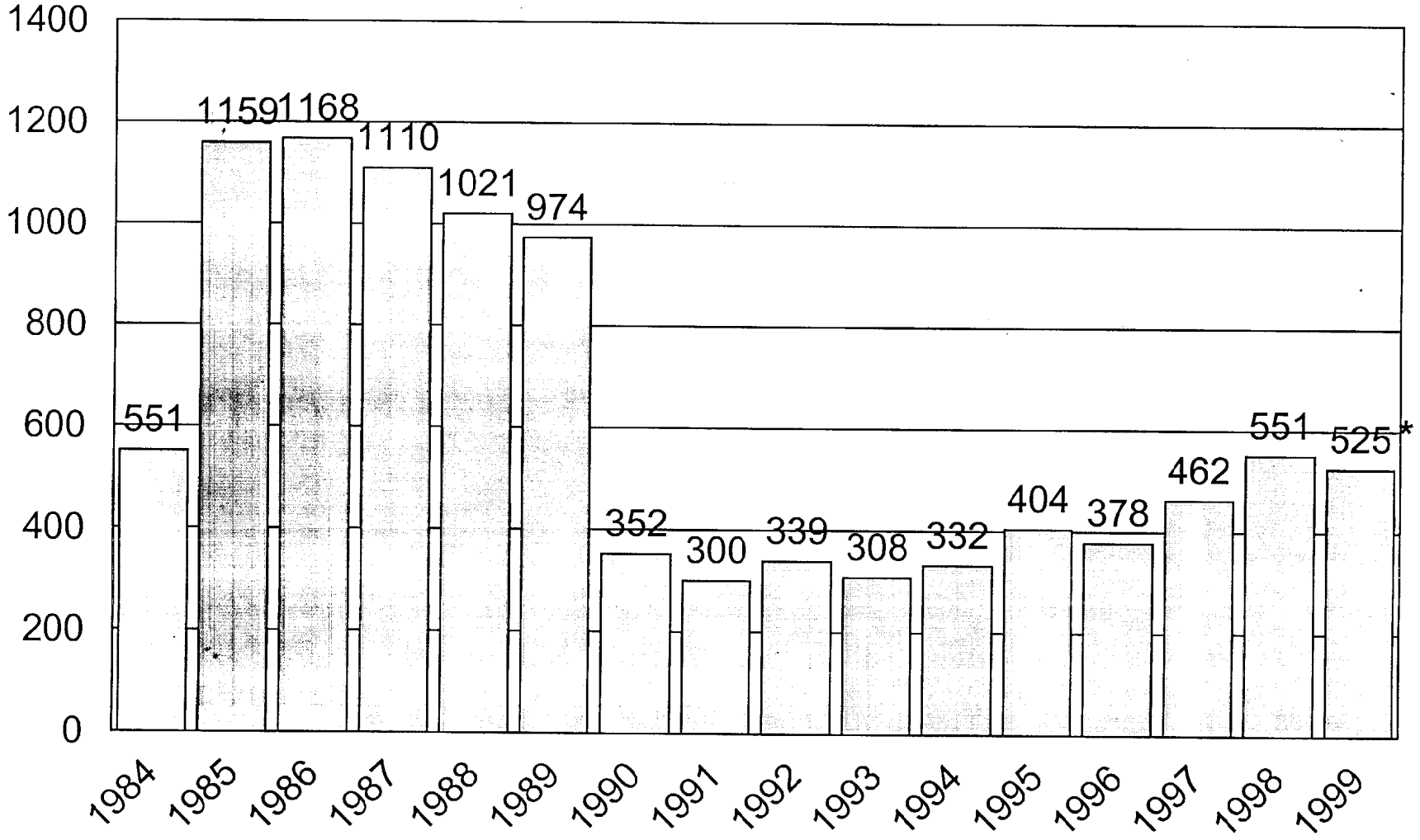
Patent Certification

- NDA filing requirements
- Patents in "Orange Book"
- Four certifications
- Use statement

When Can a Generic Drug be Marketed?

- after patent protection and/or exclusivity ends, or
- patent owner waives its rights, and
- FDA requirements are met

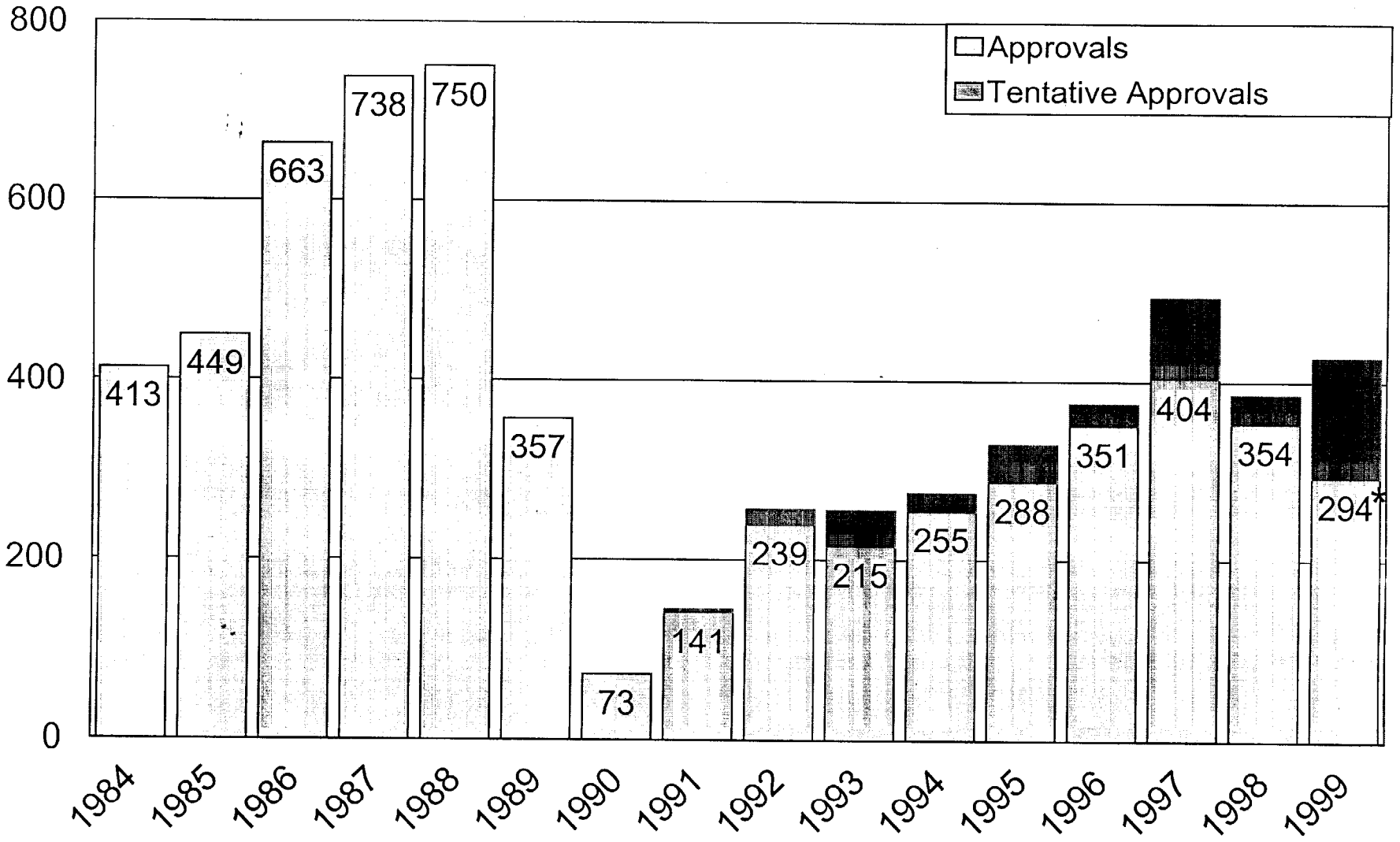
Receipts by FY Since 1984



Note: Old Counting System

* Projected

Approvals by FY Since 1984



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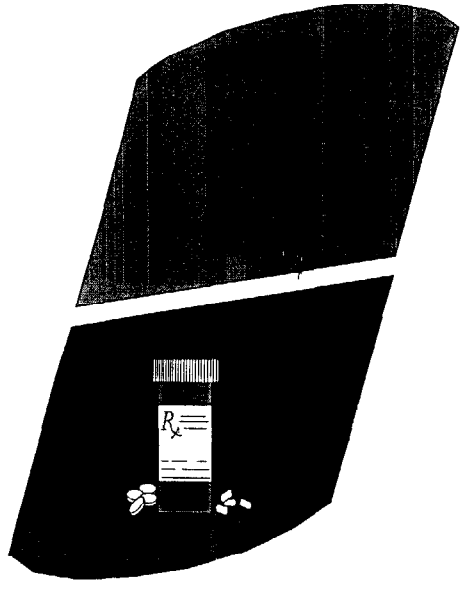

APPROVED DRUG PRODUCTS

WITH THERAPEUTIC EQUIVALENCE EVALUATIONS

19th EDITION

THE PRODUCTS IN THIS LIST HAVE BEEN APPROVED UNDER SECTIONS 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
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CENTER FOR DRUG EVALUATION AND RESEARCH
OFFICE OF INFORMATION TECHNOLOGY
DIVISION OF DATABASE MANAGEMENT AND SERVICES

1999

Approved Drug Products with Therapeutic Equivalence Evaluations "Orange Book"

- Drug products listed in the "Orange Book"
  - ▸ Approved
    - NDA's - includes antibiotics
    - ANDA's
    - AADA's

- Drug products NOT listed in the "Orange Book"
  - ▸ Pre 1938 or old drugs
  - ▸ DESI drug products for which efficacy has not been demonstrated

Orange Book

- Reference book for states, industry, and health care professionals (HMO's, hospital, some pharmacists)
- Therapeutic equivalence codes
  - "A" = substitutable
  - "B" = inequivalent, not substitutable
- Expiration dates, patent and exclusivity

CDER Coordinating Committees